## REMARKS

Claims 1-27, 30-36 and 39 are pending in the above-identified application. Applicants have reviewed the Office Action mailed June 14, 2005, and respectfully traverses all grounds for rejecting the application for the reasons that follow.

## Rejections Under 35 U.S.C. § 112

Claims 1-27 and 30-36 remain rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement allegedly because it would be unpredictable to practice the invention as claimed. The Office maintains that Lem that disruption of both alleles of the rhodopsin gene results in the failure of the ROS to form in the transgenic animals. Ryan et al. and Holschneider are again relied upon allegedly because the claims are not limited to transgene integration into the rhodopsin gene. acknowledges that routine experimentation, even if time consuming, does not constitute undue experimentation.

Applicant maintains that Lem et al. does not state or suggest that expression is unpredictable. Further, the phrase relied on by the Office also does not show unpredictability. As pointed out in Applicant's previous Response, the statement that rod outer segments may not form during later development does not change the description in Lim et al. that "mice lacking both opsin alleles initially develop normally. Abstract at page 736 (emphasis added). Such descriptions are sufficient to preclude any assertion of undue experimentation of the claimed invention.

With respect to Ryan et al. and Holschneider et al., as pointed out in Applicants' previous Response, the application teaches and the claims are directed to a gene targeting construct, a cell and a mouse produced from the claimed construct that results in the homologous recombination or site specific recombination of the transgene at the rhodopsin gene locus. In this regard, the claims recite that the transgene is flanked by 5' and 3' DNA sequences which are homologous to the mouse rhodopsin gene. These flanking sequences are sufficient to promote homologous recombination between the construct and a mouse rhodopsin gene to result in an operable association between the transgene and a rod-specific regulatory sequence. Accordingly, the

claims do recite transgene integration into the normal locus for the rhodopsin gene. In light of the above arguments, Applicants respectfully maintain that the application sufficiently teaches those skilled in the art how to make and use invention as claimed. Withdraw of this ground of rejection is respectfully requested.

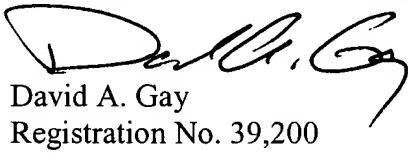
## CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned attorney if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP



David A. Gay
Registration No. 39,200

4370 La Jolla Village Drive, Suite 700
San Diego, CA 92122
Phone: 858.535.9001 DAG:gss
Facsimile: 858.597.1585
**Date: December 14, 2005**

**Please recognize our Customer No. 41552 as our correspondence address.**